

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently Amended) An implantable apparatus for infusing a plurality of medicating agents to a specific desired location at a tumor site for nonsystemic treatment of a tumor, when implanted within a patient's body, comprising:

an implantable pouch having ~~multiple~~ a plurality of collapsible and disintegratable chambers composed of a bioabsorbable material, the pouch comprising a scaffolding ~~comprised of collagen~~ forming a matrix capable of degrading over time, and a synthetic human skin for substantially enclosing the pouch, the chambers being structurally defined by the matrix, each chamber having a volume for storing a corresponding one of the plurality of the medicating agents in a macroscopic amount and for a duration effective for tumor treatment including relatively long durations, and wherein the chambers and the synthetic human skin are arranged and configured to substantially completely collapse and disintegrate within the patient's body with depletion of the plurality of medicating agents which is selectively dispensed from the chambers;

where the plurality of ~~multiple~~ medicating agents disposed are stored in said corresponding ones of the plurality of collapsible chambers;

multiple implantable piezoelectric pumps of celluloid material fabricated in the pouch which pumps forms a skeleton for the pouch, the pumps being configured to transfer the medicating agents to ~~said~~ the patient;

where the synthetic human skin is an implantable and bioabsorbable skin substitute comprising a porous matrix of fibers of cross-linked tendon collagen and a chondroitin sulfate with a layer made of synthetic polysiloxane polymer covering the pouches and pumps; and

at least one implanted sensor to measure a local homeostatic response related to at least one of the plurality of medicating agents; and

an implanted control circuit with a programmable memory on a biodegradable substrate housed within and implanted at the site of implantation of the pouch and proximate to the pumps to control optimal local ~~proper~~ dosing amounts of each of the medicating agents and scheduling of the medicating agents in a closed loop control mode so that control of the operation is performed autonomously as determined by adjustable values of locally sensed homeostatic parameters at the treatment site.

where the control circuit controls at least one of the piezoelectric pumps to modify the state of the tumor in response to measurements from the implanted sensor, and where the control circuit controls and selectively adjusts the scheduling of the amounts of the medicating agents which are delivered in response to selective user commands delivered to the control circuit and alterable during a treatment process after implantation.

2. – 3. (cancelled)

4. (previously presented) The apparatus of claim 1 where the control circuit to control the piezoelectric pumps provides for autonomously regulating, controlling, and modulating a combination therapy of cytokine and chemotherapeutic agents for the purpose of tumor elimination in a closed loop control mode.

5. (previously presented) The apparatus of claim 1 where the control circuit to control the piezoelectric pumps autonomously administers less than the maximum tolerated dose of at least one medicating agent in the closed loop control mode.

6. (original) The apparatus of claim 1, said at least one medicating agent comprising at least one of, a cytotoxic agent, a pleiotrophic agent, and an agent having both cytotoxic and pleiotrophic properties.

7. (Withdrawn) The apparatus of claim 1 further comprising control logic to control said at least one piezoelectric valve, said control logic configured to change a sequence of events, such as release of various agents on a specific schedule and dose

due to the innate capability of the apparatus to receive commands via communication links, thereby offering a treatment change in mid-stream by transmitting program codes, which instruct the microcontroller to enhance one process or another.

8. (Withdrawn)                      The apparatus of claim 1 further comprising control logic to control said at least one piezoelectric valve to regulate and schedule a dose of said medicating agent.

9. (previously amended)      The apparatus of claim 1 further comprising control logic to control said at least one piezoelectric valve to provide combination therapy for solid tumor.

10. (original) The apparatus of claim 1 further comprising control logic to control said at least one piezoelectric valve to provide selective treatment comprising at least one of:

Interferon  $\alpha$  and 5 fluorouracil and calcium liucovorin combination of dacarbazine, BCNU, cisplatin, and tonoxifen followed by interferon  $\alpha$  and IL-2.

11. (cancelled)

12. (previously amended) The apparatus of claim 1 further comprising control logic to control said at least one piezoelectric valve to control release of said medicating agent based on tumor-specific behavior.

13. (original) The apparatus of claim 1 further comprising sensors to monitor at least one of a temperature, a pH level, and a pressure in a tumor region.

14. (original) The apparatus of claim 1 further comprising sensors and control logic to monitor biometric measures and indications of the behavior of a tumor and a treatment history.

15. (original) The apparatus of claim 1 further comprising a sensor to measure pH.

16. (previously amended) The apparatus of claim 1 further comprising pressure and temperature sensors.

17. (Withdrawn) The apparatus of claim 1 further comprising a processor and software module configured to differentiate malignant versus normal cells due to lack of specificity of the cancer cell.

18. (previously amended) The apparatus of claim 1 further configured to measure pressure between a tumor site and the pouch.

19. (Withdrawn) The apparatus of claim 1 further comprising logic to administer said medicating agent on schedule as well as duration and sequence.

20. (Withdrawn) The apparatus of claim 1 configured to deliver said medicating agent by the use of electronic control of said piezoelectric pump.

21. (original) The apparatus of claim 1 further configured to provide infusion of biological response modifiers in combination with chemotherapeutic agents.

22. (original) The apparatus of claim 1 wherein said piezoelectric pump comprises a piezoelectric layer-wise pump and valve.

23. (Withdrawn)                    The apparatus of claim 1 further comprising an electronic control module to control said piezoelectric pump to provide timed release of said medicating agent.

24. (previously amended)    The apparatus of claim 1 further comprising a software module to control said piezoelectric pump.

25. (previously amended)    The apparatus of claim 1 further comprising a software module to control said piezoelectric pump to provide for controlled-delivery of the multiple medicating agents.

26. (Withdrawn)                    The apparatus of claim 1 further supports controlled delivery of chemotherapeutic agents and BRMs which is achieved by the use of an electronic timer and a microcontroller.

27. (Withdrawn)                    The apparatus of claim 1 further comprising a software module to control said piezoelectric pump to provide an apparatus having multiple

chambers, providing the clinician the ability to deliver a set of multiple medicating agents to the tumor site.

28. (original) The apparatus of claim 1 further comprising a software module to control said piezoelectric pump to provide an irrigation action which allows for the bioavailability of said medicating agent.

29. (previously amended) The apparatus of claim 1 further comprising a software module to control said piezoelectric pump to provide an irrigation action for delivery of said medicating agent to provide improved penetration and treatment of tumors.

30. (original) The apparatus of claim 1 further comprising a software module to control said piezoelectric pump to provide an irrigation action for delivery of said medicating agent to refractory nature of a tumor by enhancing angiogenetic action at the tumor site.

31. (Withdrawn) The apparatus of claim 1 further comprising a software module to control said piezoelectric pump to provide an active pump and valve to provide control of dosage and timing of the medicating agent.



32. (original) The apparatus of claim 1 further comprising a communications link.

33. (previously presented) The apparatus of claim 3 further comprising an implantable wireless bi-directional communications link coupled to the implanted sensor through the implanted control circuit and for communication of local homeostatic sensed bio-parameters to an external user.

34. (Withdrawn)                      The apparatus of claim 1 further comprising a digital communications link.

35. (Withdrawn)                      The apparatus of claim 1 further comprising an RF communications link.

36. (Withdrawn)                      The apparatus of claim 1 further comprising a communications link to provide control instructions to said piezoelectric valve.

37. (previously amended) The apparatus of claim 1., where the piezoelectric pump comprises comprising a pressure generator to develop pressure along an axial path of an electrostatic valve.

38. (previously amended) The apparatus of claim 1 comprising the scaffolding to reduce clogging of the piezoelectric pump with increased flow of the medicating agent.

39. (original) The apparatus of claim 1 further comprising a pressure monitor.

40. (cancelled)

41. (original) The apparatus of claim 1 further comprising a control module to provide a voltage control of said piezoelectric pump.

42. (original) The apparatus of claim 1, said piezoelectric pump comprising a bimorph geometry.

43. (Cancelled)

44. (Withdrawn)           The apparatus of claim 1 further supports system where a continuous monitoring and reporting of biological response parameters are maintained in the resident memory of the system.

45. (Withdrawn)           The apparatus of claim 1 further comprising a control system to control delivery of said medicating agent on a case-specific basis using a pre-programmed dosing schedule.

46. (Withdrawn)           The apparatus of claim 1 further comprising a control system to control delivery of said medicating agent based on look-up-tables.

47. (original) The apparatus of claim 1 further comprising a control system to control delivery of said medicating agent in real time.

48. (Withdrawn)                      The apparatus of claim 1 wherein said pump comprises a valve, said apparatus further comprising control logic to regulate the dispensation of medicating agent by modifying the duty cycle of the valve.

49. (Withdrawn)                      The apparatus of claim 1 further comprising control logic to regulate deliver of said medicating agent based on a pleiotrophic nature of said medicating agent.

50. (Withdrawn)                      The apparatus of claim 1 further comprising control logic to schedule delivery of said medicating agent based on toxicity and to allow for measures such as bioavailability, solubility, concentration, and circulation based on locality.

51. (original) The apparatus of claim 1 wherein said medicating agent comprises biomodulators.

52. (Withdrawn)                      The apparatus of claim 1 comprising control logic to deliver said medicating agent based on individual difference of different tumors.

53. (Withdrawn) The apparatus of claim 1 further supports the ability of the apparatus to mitigate the known factors such as peak serum concentration.

54. (Withdrawn) The apparatus of claim 1 further configured to evaluate the effectiveness of the medicating agent used during animal and clinical studies by providing the details and feedback on the use, dose, cycle, circadian time effects and the entire pharmacokinetic, as well as pharmacodynamic behavior of the medicating agents.

55. (previously amended) The apparatus of claim 1 further configured to be implanted in the neighborhood of the tumor site for effective local delivery of the medicating agents.

56. (original) The apparatus of claim 1 further configured to provide a local administration of BRMs and chemotherapeutic agents to enhance mechanisms that support overlapping effects in reducing tumor burden and elimination of tumors.

57. (original) The apparatus of claim 1 comprising a plurality of medicating agents for combination therapy, using one or more biological response modifiers to modify the

relationship between tumor and host, hence modifying the host's biological response to tumor cells and chemotherapeutic agents.

58. (Withdrawn)                      The apparatus of claim 1, further comprising control logic to deliver said medicating agent by modulating the pharmacokinetics of the medicating agent as key enzymes, attenuation of drug resistance mechanisms, and modifications in permeability of the vascular system which allow increased accumulation of chemotherapeutic drugs at the tumor site, causing reduction of tumor burden.

59. (Withdrawn)                      The apparatus of claim 1 further supports the use of such modality to improve anti-tumor response and to increase production of cytokines, thereby decreasing suppressor mechanisms.

60. (Withdrawn)                      The apparatus of claim 1 comprising control logic to supports modalities of a patient's tolerance to cytotoxic effects.

61. (Withdrawn)                      The apparatus of claim 1 further comprising a software module to control said piezoelectric pump to provide an apparatus to provide a dose and timeline to produce tumor burden elimination or reduction.

62. - 64. (cancelled)